

APPLICANTS: **Gaston and Stamler**  
U.S.N.: **10/772,374**

## **REMARKS**

Claims 1 and 9 are pending in the application. No new matter is added.

In support of the remarks and arguments stated *infra*, Applicants have submitted herewith the Declaration of Dr. Jonathan S. Stamler and Dr. Benjamin Gaston under 37 C.F.R. §1.132 (“Stamler and Gaston Declaration”) which was originally submitted in U.S. Patent Application 10/380,763, now U.S. Patent No. 6,723,703. The present application is a continuation application of U.S. Patent No. 6,723,703.

### **Rejection under 35 U.S.C. §103**

Claims 1 and 9 are rejected under 35 U.S.C. §103(a), as being unpatentable over U.S. Patent 6,331,543 to Garvey (“Garvey”) in view of U.S. Patent 6,331,543 to Stamler (“Stamler”). *See*, Office Action at pages 3-5. Applicants traverse.

It is well recognized under U.S. law, that any rejection of a claim for obviousness over a combination of prior art references must establish that: (1) the combination produces the claimed invention; and (2) the prior art contains a suggestion or motivation to combine the prior art references in such a way as to achieve the claimed invention. *See*, In re Vaeck, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). The motivation to modify the prior art must flow from some teaching in the art that suggests the desirability or incentive to make the modification needed to arrive at the claimed invention. *See*, In re Napier, 34 U.S.P.Q.2d 1782, 1784 (Fed. Cir. 1995). The mere fact that the prior art could be modified does not make the modification obvious unless the prior art suggests the desirability of the modification. *See*, In re Laskowski, 10 U.S.P.Q.2d 1397, 1399 (Fed. Cir. 1989).

The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. *See*, In re Dow Chemical Co., 837 F.2d 469 (Fed. Cir. 1988). Evidence showing there was no reasonable expectation of success may support a conclusion of nonobviousness. *See*, In re Rinehart, 531 F.2d 1048, 189 USPQ 143 (CCPA 1976). Whether an art is predictable or whether the proposed

APPLICANTS:      **Gaston and Stamler**  
U.S.S.N.:        **10/772,374**

modification or combination of the prior art has a reasonable expectation of success is determined at the time the invention was made. *See, Ex parte Erlich*, 3 USPQ2d 1011 (Bd. Pat. App. & Inter. 1986). Further, it is also well recognized that a prior art reference must be considered in its entirety, *i.e.*, as a whole, including portions that would lead away from the claimed invention. *See, W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). Moreover, a reasonable expectation of success requires that the guidance provided by the reference must be sufficiently specific to direct the attention to one skilled in the art to the selection of parameters and choices necessary to obtain the invention. *See, In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988). Prior art does not satisfy this requirement if it is necessary to vary all parameters, or to try each of numerous possible choices, in order possibly to arrive at successful results. *See, Id.*

Applicants submit that the prior art does not contain a suggestion or motivation to combine the prior art references of Garvey and Stamler to achieve the present invention and that there is no reasonable expectation of success combining the teachings of Garvey and Stamler to reach the present invention. More specifically, Applicants submit that Garvey is defective for the teachings relied upon by the Examiner in asserting the rejection and that one of ordinary skill in the art would have no desire or motivation to combine these defective teachings with the teachings of Stamler and would have no reasonable expectation of success combining the references to reach the present invention.

Garvey has no specific working examples directed to treating a patient with cystic fibrosis. It mentions cystic fibrosis among a laundry list of disorders which it characterizes as diseases induced by increased metabolism of cGMP. Garvey mentions as one alternative a composition comprising a PDE inhibitor and at least one compound that donates, transfers or releases nitrogen monoxide as a charged species. *See, Garvey* at column 3, lines 38-50. Garvey then broadly teaches that all the disclosed compounds and compositions can be utilized in methods to treat any diseases induced by the increased metabolism of cGMP. Garvey does not point to any specific compounds or compositions to treat cystic fibrosis. Thus, for Garvey to treat cystic fibrosis with an NO donor, one or ordinary skill in the art must select a specific alternative where NO is used and one must select cystic fibrosis for a disease to treat. Consider also that claim 66 of Garvey does not include cystic fibrosis among the disorders listed. It is

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U.S.S.N.:        **10/772,374**

submitted that this suggests that the PTO or the inventors considered the disclosure of Garvey as not enabling the treatment of cystic fibrosis. A non-enabled disclosure cannot provide anticipation and cannot be the basis for an obviousness rejection. In re Hoecksema, 158 U.S.P.Q. 596, 601 (CCPA 1968).

Furthermore, Applicants submit that Garvey has incorrectly described cystic fibrosis as being a disease induced by increased metabolism of cGMP. Garvey lists U.S. 5,849,741, U.S. 5,869,486, WO 98/49166 and WO 97/03985 as the only support for the characterization of cystic fibrosis as being a disease induced by increased metabolism of cGMP but these four documents do not mention cystic fibrosis.

The obviousness rejection relies on Garvey as teaching administering NO donors in treatment of cystic fibrosis. It is submitted that this underlying threshold of the rejection is defective because one skilled in the art on considering Garvey, would not believe that the method of Garvey would be beneficial in the treatment of cystic fibrosis because cystic fibrosis is not induced by increased metabolism of cGMP and one skilled in the art would know this even though Garvey lists cystic fibrosis as a disorder induced by metabolism of cGMP. *See, Stamler and Gaston Declaration* at ¶10. The Stamler and Gaston Declaration is consistent with the disclosures of U.S. 5,849,741, U.S. 5,869,486, WO 98/49166 and WO 97/03985.

Stamler does not cure the deficiencies of Garvey. The obviousness rejection relies on Stamler as showing that inhalation of a nebulized nitric oxide donor where the donor is present as solid or liquid particles was known. It is submitted that this position is defective because Stamler does not disclose administration of solid or liquid particles of an NO donor or other agent for the treatment of cystic fibrosis. The recitation of U.S. 6,314,956 B1 at column 1, lines 27-44 was included as a basis for distinguishing U.S. Patent No. 5,823,180 issued to Zapol (“Zapol”) which uses an aerosol to treat pulmonary vasoconstriction and asthma, and therefore does not suggest this regimen for treating cystic fibrosis. Note that Zapol does not mention cystic fibrosis in its list of disorders treated. *See, Zapol*, column 4, lines 44-61.

Thus, one of ordinary skill in the art reading Garvey, as a whole, would not be motivated to combine the teachings of Garvey with the teachings of Stamler to reach the present invention. Further, Applicants submit that one of ordinary skill in the art would recognize that the

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U.S.S.N.: **10/772,374**

combination of the teachings of Garvey and Stamler would not provide a reasonable expectation of success in achieving the claimed invention.

Reconsideration and withdrawal of the present rejections is respectfully requested.

**Double Patenting Rejections**

Claims 1 and 9 are rejected under the judicially created doctrine of obvious-type double patenting, as being unpatentable over claims 1, 2, 14 and 15 of U.S. Patent No. 6,627,602.

Applicants disagree. However, in the interest of expediting prosecution of the present application, Applicants file herewith a terminal disclaimer in compliance with 37 C.F.R. §1.321(c). Withdrawal of this rejection is respectfully requested.

**CONCLUSION**

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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